

SEQUENCE LISTING

<110> Cheever, Martin A.
Gheysen, Dirk
Corixa Corporation
SmithKline Beecham Biologicals S. A.

<120> HER-2/neu Fusion Proteins

<130> 014058-009810PC

<140> US 09/493,480

<141> 2000-01-28

<150> US 60/117,976

<151> 1999-01-29

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<170> PatentIn Ver. 2.1

<210> 1

<211> 1255

<212> PRT

<213> Homo sapiens

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<223> human HER-2/neu protein

<220>

<221> DOMAIN

<222> (1)..(653)

<223> extracellular domain (ECD)

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<222> (676)..(1255)

<223> intracellular domain (ICD)

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<223> phosphorylation domain (PD)

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<222> (990)..(1048)

<223> fragment of the phosphorylation domain, preferred
portion (delta PD)

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Express Mail No.
EL 827035155 US

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125
 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140
 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160
 Leu Cys Tyr Gln Asp Thr-Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175
 Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190
 His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205
 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220
 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240
 Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255
 His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270
 Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365

005050: 95275860

Arg	Leu	Leu	Gln	Glu	Thr	Glu	Leu	Val	Glu	Pro	Leu	Thr	Pro	Ser	Gly	690	695	700	
Ala	Met	Pro	Asn	Gln	Ala	Gln	Met	Arg	Ile	Leu	Lys	Glu	Thr	Glu	Leu	705	710	715	720
Arg	Lys	Val	Lys	Val	Leu	Gly	Ser	Gly	Ala	Phe	Gly	Thr	Val	Tyr	Lys	725	730	735	
Gly	Ile	Trp	Ile	Pro	Asp	Gly	Glu	Asn	Val	Lys	Ile	Pro	Val	Ala	Ile	740	745	750	
Lys	Val	Leu	Arg	Glu	Asn	Thr	Ser	Pro	Lys	Ala	Asn	Lys	Glu	Ile	Leu	755	760	765	
Asp	Glu	Ala	Tyr	Val	Met	Ala	Gly	Val	Gly	Ser	Pro	Tyr	Val	Ser	Arg	770	775	780	
Leu	Leu	Gly	Ile	Cys	Leu	Thr	Ser	Thr	Val	Gln	Leu	Val	Thr	Gln	Leu	785	790	795	800
Met	Pro	Tyr	Gly	Cys	Leu	Leu	Asp	His	Val	Arg	Glu	Asn	Arg	Gly	Arg	805	810	815	
Leu	Gly	Ser	Gln	Asp	Leu	Leu	Asn	Trp	Cys	Met	Gln	Ile	Ala	Lys	Gly	820	825	830	
Met	Ser	Tyr	Leu	Glu	Asp	Val	Arg	Leu	Val	His	Arg	Asp	Leu	Ala	Ala	835	840	845	
Arg	Asn	Val	Leu	Val	Lys	Ser	Pro	Asn	His	Val	Lys	Ile	Thr	Asp	Phe	850	855	860	
Gly	Leu	Ala	Arg	Leu	Leu	Asp	Ile	Asp	Glu	Thr	Glu	Tyr	His	Ala	Asp	865	870	875	880
Gly	Gly	Lys	Val	Pro	Ile	Lys	Trp	Met	Ala	Leu	Glu	Ser	Ile	Leu	Arg	885	890	895	
Arg	Arg	Phe	Thr	His	Gln	Ser	Asp	Val	Trp	Ser	Tyr	Gly	Val	Thr	Val	900	905	910	
Trp	Glu	Leu	Met	Thr	Phe	Gly	Ala	Lys	Pro	Tyr	Asp	Gly	Ile	Pro	Ala	915	920	925	
Arg	Glu	Ile	Pro	Asp	Leu	Leu	Glu	Lys	Gly	Glu	Arg	Leu	Pro	Gln	Pro	930	935	940	
Pro	Ile	Cys	Thr	Ile	Asp	Val	Tyr	Met	Ile	Met	Val	Lys	Cys	Trp	Met	945	950	955	960
Ile	Asp	Ser	Glu	Cys	Arg	Pro	Arg	Phe	Arg	Glu	Leu	Val	Ser	Glu	Phe	965	970	975	
Ser	Arg	Met	Ala	Arg	Asp	Pro	Gln	Arg	Phe	Val	Val	Ile	Gln	Asn	Glu	980	985	990	
Asp	Leu	Gly	Pro	Ala	Ser	Pro	Leu	Asp	Ser	Thr	Phe	Tyr	Arg	Ser	Leu	995	1000	1005	

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
1010 1015 1020

Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
1025 1030 1035 1040

Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
1045 1050 1055

Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
1060 1065 1070

Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
1075 1080 1085

Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
1090 1095 1100

Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
1105 1110 1115 1120

Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
1125 1130 1135

Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
1140 1145 1150

Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
1155 1160 1165

Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
1170 1175 1180

Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
1185 1190 1195 1200

Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
1205 1210 1215

Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
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Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
1235 1240 1245

Leu Gly Leu Asp Val Pro Val
1250 1255

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<211> 1256

<212> PRT

<213> Rattus sp.

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<223> rat HER-2/neu protein

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<221> DOMAIN

<222> (1)..(654)

<223> extracellular domain (ECD)

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225					230					235					240
Cys	Ala	Ala	Gly	Cys	Thr	Gly	Pro	Lys	His	Ser	Asp	Cys	Leu	Ala	Cys
				245					250					255	
Leu	His	Phe	Asn	His	Ser	Gly	Ile	Cys	Glu	Leu	His	Cys	Pro	Ala	Leu
			260					265					270		
Val	Thr	Tyr	Asn	Thr	Asp	Thr	Phe	Glu	Ser	Met	His	Asn	Pro	Glu	Gly
		275					280					285			
Arg	Tyr	Thr	Phe	Gly	Ala	Ser	Cys	Val	Thr	Thr	Cys	Pro	Tyr	Asn	Tyr
	290					295					300				
Leu	Ser	Thr	Glu	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Pro	Asn	Asn
305					310					315					320
Gln	Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser
				325					330					335	
Lys	Pro	Cys	Ala	Arg	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg
			340					345					350		
Gly	Ala	Arg	Ala	Ile	Thr	Ser	Asp	Asn	Val	Gln	Glu	Phe	Asp	Gly	Cys
		355					360					365			
Lys	Lys	Ile	Phe	Gly	Ser	Leu	Ala	Phe	Leu	Pro	Glu	Ser	Phe	Asp	Gly
	370					375					380				
Asp	Pro	Ser	Ser	Gly	Ile	Ala	Pro	Leu	Arg	Pro	Glu	Gln	Leu	Gln	Val
385					390					395					400
Phe	Glu	Thr	Leu	Glu	Glu	Ile	Thr	Gly	Tyr	Leu	Tyr	Ile	Ser	Ala	Trp
				405					410					415	
Pro	Asp	Ser	Leu	Arg	Asp	Leu	Ser	Val	Phe	Gln	Asn	Leu	Arg	Ile	Ile
			420					425					430		
Arg	Gly	Arg	Ile	Leu	His	Asp	Gly	Ala	Tyr	Ser	Leu	Thr	Leu	Gln	Gly
		435					440					445			
Leu	Gly	Ile	His	Ser	Leu	Gly	Leu	Arg	Ser	Leu	Arg	Glu	Leu	Gly	Ser
	450					455					460				
Gly	Leu	Ala	Leu	Ile	His	Arg	Asn	Ala	His	Leu	Cys	Phe	Val	His	Thr
465					470					475					480
Val	Pro	Trp	Asp	Gln	Leu	Phe	Arg	Asn	Pro	His	Gln	Ala	Leu	Leu	His
				485					490					495	
Ser	Gly	Asn	Arg	Pro	Glu	Glu	Asp	Cys	Gly	Leu	Glu	Gly	Leu	Val	Cys
			500					505					510		
Asn	Ser	Leu	Cys	Ala	His	Gly	His	Cys	Trp	Gly	Pro	Gly	Pro	Thr	Gln
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105050-9524330

Cys	Val	Asn	Cys	Ser	His	Phe	Leu	Arg	Gly	Gln	Glu	Cys	Val	Glu	Glu	530	535	540
Cys	Arg	Val	Trp	Lys	Gly	Leu	Pro	Arg	Glu	Tyr	Val	Ser	Asp	Lys	Arg	545	550	555
Cys	Leu	Pro	Cys	His	Pro	Glu	Cys	Gln	Pro	Gln	Asn	Ser	Ser	Glu	Thr	565	570	575
Cys	Phe	Gly	Ser	Glu	Ala	Asp	Gln	Cys	Ala	Ala	Cys	Ala	His	Tyr	Lys	580	585	590
Asp	Ser	Ser	Ser	Cys	Val	Ala	Arg	Cys	Pro	Ser	Gly	Val	Lys	Pro	Asp	595	600	605
Leu	Ser	Tyr	Met	Pro	Ile	Trp	Lys	Tyr	Pro	Asp	Glu	Glu	Gly	Ile	Cys	610	615	620
Gln	Pro	Cys	Pro	Ile	Asn	Cys	Thr	His	Ser	Cys	Val	Asp	Leu	Asp	Glu	625	630	635
Arg	Gly	Cys	Pro	Ala	Glu-Gln	Arg	Ala	Ser	Pro	Val	Thr	Phe	Ile	Ile		645	650	655
Ala	Thr	Val	Glu	Gly	Val	Leu	Leu	Phe	Leu	Ile	Leu	Val	Val	Val	Val	660	665	670
Gly	Ile	Leu	Ile	Lys	Arg	Arg	Arg	Gln	Lys	Ile	Arg	Lys	Tyr	Thr	Met	675	680	685
Arg	Arg	Leu	Leu	Gln	Glu	Thr	Glu	Leu	Val	Glu	Pro	Leu	Thr	Pro	Ser	690	695	700
Gly	Ala	Met	Pro	Asn	Gln	Ala	Gln	Met	Arg	Ile	Leu	Lys	Glu	Thr	Glu	705	710	715
Leu	Arg	Lys	Val	Lys	Val	Leu	Gly	Ser	Gly	Ala	Phe	Gly	Thr	Val	Tyr	725	730	735
Lys	Gly	Ile	Trp	Ile	Pro	Asp	Gly	Glu	Asn	Val	Lys	Ile	Pro	Val	Ala	740	745	750
Ile	Lys	Val	Leu	Arg	Glu	Asn	Thr	Ser	Pro	Lys	Ala	Asn	Lys	Glu	Ile	755	760	765
Leu	Asp	Glu	Ala	Tyr	Val	Met	Ala	Gly	Val	Gly	Ser	Pro	Tyr	Val	Ser	770	775	780
Arg	Leu	Leu	Gly	Ile	Cys	Leu	Thr	Ser	Thr	Val	Gln	Leu	Val	Thr	Gln	785	790	795
Leu	Met	Pro	Tyr	Gly	Cys	Leu	Leu	Asp	His	Val	Arg	Glu	His	Arg	Gly	805	810	815
Arg	Leu	Gly	Ser	Gln	Asp	Leu	Leu	Asn	Trp	Cys	Val	Gln	Ile	Ala	Lys	820	825	830
Gly	Met	Ser	Tyr	Leu	Glu	Asp	Val	Arg	Leu	Val	His	Arg	Asp	Leu	Ala	835	840	845

Ala	Arg	Asn	Val	Leu	Val	Lys	Ser	Pro	Asn	His	Val	Lys	Ile	Thr	Asp
850						855					860				
Phe	Gly	Leu	Ala	Arg	Leu	Leu	Asp	Ile	Asp	Glu	Thr	Glu	Tyr	His	Ala
865					870					875					880
Asp	Gly	Gly	Lys	Val	Pro	Ile	Lys	Trp	Met	Ala	Leu	Glu	Ser	Ile	Leu
			885						890					895	
Arg	Arg	Arg	Phe	Thr	His	Gln	Ser	Asp	Val	Trp	Ser	Tyr	Gly	Val	Thr
			900					905					910		
Val	Trp	Glu	Leu	Met	Thr	Phe	Gly	Ala	Lys	Pro	Tyr	Asp	Gly	Ile	Pro
		915					920					925			
Ala	Arg	Glu	Ile	Pro	Asp	Leu	Leu	Glu	Lys	Gly	Glu	Arg	Leu	Pro	Gln
	930					935					940				
Pro	Pro	Ile	Cys	Thr	Ile	Asp	Val	Tyr	Met	Ile	Met	Val	Lys	Cys	Trp
945					950					955					960
Met	Ile	Asp	Ser	Glu	Cys	Arg	Pro	Arg	Phe	Arg	Glu	Leu	Val	Ser	Glu
				965					970					975	
Phe	Ser	Arg	Met	Ala	Arg	Asp	Pro	Gln	Arg	Phe	Val	Val	Ile	Gln	Asn
			980					985					990		
Glu	Asp	Leu	Gly	Pro	Ser	Ser	Pro	Met	Asp	Ser	Thr	Phe	Tyr	Arg	Ser
		995					1000					1005			
Leu	Leu	Glu	Asp	Asp	Asp	Met	Gly	Asp	Leu	Val	Asp	Ala	Glu	Glu	Tyr
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Leu	Val	Pro	Gln	Gln	Gly	Phe	Phe	Ser	Pro	Asp	Pro	Thr	Pro	Gly	Thr
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Gly	Ser	Thr	Ala	His	Arg	Arg	His	Arg	Ser	Ser	Ser	Thr	Arg	Ser	Gly
			1045					1050					1055		
Gly	Gly	Glu	Leu	Thr	Leu	Gly	Leu	Glu	Pro	Ser	Glu	Glu	Gly	Pro	Pro
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Arg	Ser	Pro	Leu	Ala	Pro	Ser	Glu	Gly	Ala	Gly	Ser	Asp	Val	Phe	Asp
	1075						1080					1085			
Gly	Asp	Leu	Ala	Met	Gly	Val	Thr	Lys	Gly	Leu	Gln	Ser	Leu	Ser	Pro
	1090					1095					1100				
His	Asp	Leu	Ser	Pro	Leu	Gln	Arg	Tyr	Ser	Glu	Asp	Pro	Thr	Leu	Pro
1105				1110						1115					1120
Leu	Pro	Pro	Glu	Thr	Asp	Gly	Tyr	Val	Ala	Pro	Leu	Ala	Cys	Ser	Pro
			1125					1130					1135		
Gln	Pro	Glu	Tyr	Val	Asn	Gln	Ser	Glu	Val	Gln	Pro	Gln	Pro	Pro	Leu
		1140					1145					1150			
Thr	Pro	Glu	Gly	Pro	Leu	Pro	Pro	Val	Arg	Pro	Ala	Gly	Ala	Thr	Leu
	1155						1160					1165			

Asn	Gln	Leu	Ala	Leu	Thr	Leu	Ile	Asp	Thr	Asn	Arg	Ser	Arg	Ala	Cys	
			180					185						190		
His	Pro	Cys	Ser	Pro	Met	Cys	Lys	Gly	Ser	Arg	Cys	Trp	Gly	Glu	Ser	
		195					200					205				
Ser	Glu	Asp	Cys	Gln	Ser	Leu	Thr	Arg	Thr	Val	Cys	Ala	Gly	Gly	Cys	
	210					215					220					
Ala	Arg	Cys	Lys	Gly	Pro	Leu	Pro	Thr	Asp	Cys	Cys	His	Glu	Gln	Cys	
225					230					235					240	
Ala	Ala	Gly	Cys	Thr	Gly	Pro	Lys	His	Ser	Asp	Cys	Leu	Ala	Cys	Leu	
				245					250					255		
His	Phe	Asn	His	Ser	Gly	Ile	Cys	Glu	Leu	His	Cys	Pro	Ala	Leu	Val	
			260					265						270		
Thr	Tyr	Asn	Thr	Asp	Thr	Phe	Glu	Ser	Met	Pro	Asn	Pro	Glu	Gly	Arg	
		275					280					285				
Tyr	Thr	Phe	Gly	Ala	Ser	Cys	Val	Thr	Ala	Cys	Pro	Tyr	Asn	Tyr	Leu	
	290					295					300					
Ser	Thr	Asp	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Leu	His	Asn	Gln	
305					310					315					320	
Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser	Lys	
				325					330					335		
Pro	Cys	Ala	Arg	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg	Glu	
			340					345						350		
Val	Arg	Ala	Val	Thr	Ser	Ala	Asn	Ile	Gln	Glu	Phe	Ala	Gly	Cys	Lys	
		355					360					365				
Lys	Ile	Phe	Gly	Ser	Leu	Ala	Phe	Leu	Pro	Glu	Ser	Phe	Asp	Gly	Asp	
	370					375					380					
Pro	Ala	Ser	Asn	Thr	Ala	Pro	Leu	Gln	Pro	Glu	Gln	Leu	Gln	Val	Phe	
385					390					395					400	
Glu	Thr	Leu	Glu	Glu	Ile	Thr	Gly	Tyr	Leu	Tyr	Ile	Ser	Ala	Trp	Pro	
			405					410						415		
Asp	Ser	Leu	Pro	Asp	Leu	Ser	Val	Phe	Gln	Asn	Leu	Gln	Val	Ile	Arg	
			420					425						430		
Gly	Arg	Ile	Leu	His	Asn	Gly	Ala	Tyr	Ser	Leu	Thr	Leu	Gln	Gly	Leu	
		435					440						445			
Gly	Ile	Ser	Trp	Leu	Gly	Leu	Arg	Ser	Leu	Arg	Glu	Leu	Gly	Ser	Gly	
	450					455					460					
Leu	Ala	Leu	Ile	His	His	Asn	Thr	His	Leu	Cys	Phe	Val	His	Thr	Val	
465					470					475					480	
Pro	Trp	Asp	Gln	Leu	Phe	Arg	Asn	Pro	His	Gln	Ala	Leu	Leu	His	Thr	
				485					490					495		

Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr
115 120 125

Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys
130 135 140

Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro
145 150 155 160

Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala
165 170 175

Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val
180 185 190

Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu
195 200 205

Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe
210 215 220

Ser Pro Ala Phe Asp Asn-Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu
225 230 235 240

Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn
245 250 255

Pro Glu Tyr Leu Gly Leu Asp Val Pro Val
260 265

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<211> 59

<212> PRT

<213> Homo sapiens

<220>

<223> fragment of the phosphorylation domain, preferred
portion (delta PD) of human HER-2/neu

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Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr
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Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu
20 25 30

Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro
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Gly Ala Gly Gly Met Val His His Arg His Arg
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<210> 6

<211> 919

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: fusion protein
of ECD and PD of human HER-2/neu

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300

<210> 7
 <211> 712
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fusion protein
 of ECD and delta PD of human HER-2/neu

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Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
 20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
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 cagaagatcc ggaagtatac catgcgtagg ctgctgcagg agaccgagct ggtggagccg 2100
 ctgacgcccc gtggagctgt gcccacccag gctcagatgc ggatcctaaa ggagacagag 2160
 ctaaggaagc tgaaggtgct tgggtcagga gccttcggca ctgtctacaa gggcatctgg 2220
 atcccagatg gggagaacgt gaaaatcccc gtggccatca aggtgttgag ggaaaacaca 2280
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 ctctattact gggaccagaa ctcatcggag cagggtcctc caccaagtac ctttgaaggg 3720
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<210> 12
 <211> 28
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:5' primer for
 mouse HER-2/neu amplification

<400> 12
 ccatggagct ggcggcctgg tgccgttg 28

<210> 13
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:3' primer for
 mouse HER-2/neu amplification

<400> 13
 ggccttctgg ttcatactgg cacatccagg c 31

<210> 14
 <211> 1256
 <212> PRT
 <213> Mus sp.

<220>
 <223> mouse HER-2/neu protein

<400> 14
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 1 5 10 15
 Ser Pro Gly Ala Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys
 20 25 30
 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60

Leu Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Met Leu Ile Ala His Asn Arg Val Lys His Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Leu Asp Asn Val Thr Thr
 115 120 125
 Ala Ala Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
 130 135 140
 Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
 145 150 155 160
 Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Leu Arg Lys
 165 170 175
 Asn Asn Gln Leu Ala Pro Val Asp Met Asp Thr Asn Arg Ser Arg Ala
 180 185 190
 Cys Pro Pro Cys Ala Pro Thr Cys Lys Asp Asn His Cys Trp Gly Glu
 195 200 205
 Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
 210 215 220
 Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
 225 230 235 240
 Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
 245 250 255
 Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
 260 265 270
 Ile Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Leu Asn Pro Glu Gly
 275 280 285
 Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
 290 295 300
 Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
 305 310 315 320
 Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
 325 330 335
 Lys Pro Cys Ala Gly Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
 340 345 350
 Gly Ala Arg Ala Ile Thr Ser Asp Asn Ile Gln Glu Phe Ala Gly Cys
 355 360 365
 Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
 370 375 380

00854356 05090

Asn Pro Ser Ser Gly Val Ala Pro Leu Lys Pro Glu His Leu Gln Val
 385 390 395 400
 Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
 405 410 415
 Pro Glu Ser Phe Gln Asp Leu Ser Val Phe Gln Asn Leu Arg Val Ile
 420 425 430
 Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
 435 440 445
 Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
 450 455 460
 Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr
 465 470 475 480
 Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
 485 490 495
 Ser Gly Asn Arg Pro Glu Glu Ala Cys Gly Leu Glu Gly Leu Val Cys
 500 505 510
 Asn Ser Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln
 515 520 525
 Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
 530 535 540
 Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Arg Gly Lys His
 545 550 555 560
 Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
 565 570 575
 Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys
 580 585 590
 Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
 595 600 605
 Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
 610 615 620
 Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
 625 630 635 640
 Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
 645 650 655
 Ala Thr Val Val Gly Val Leu Leu Phe Leu Ile Ile Val Val Val Ile
 660 665 670
 Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
 675 680 685
 Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
 690 695 700

Gly	Ala	Val	Pro	Asn	Gln	Ala	Gln	Met	Arg	Ile	Leu	Lys	Glu	Thr	Glu	
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				725					730						735	
Lys	Gly	Ile	Trp	Ile	Pro	Asp	Gly	Glu	Asn	Val	Lys	Ile	Pro	Val	Ala	
			740					745						750		
Ile	Lys	Val	Leu	Arg	Glu	Asn	Thr	Ser	Pro	Lys	Ala	Asn	Lys	Glu	Ile	
		755					760						765			
Leu	Asp	Glu	Ala	Tyr	Val	Met	Ala	Gly	Val	Gly	Ser	Pro	Tyr	Val	Ser	
	770					775					780					
Arg	Leu	Leu	Gly	Ile	Cys	Leu	Thr	Ser	Thr	Val	Gln	Leu	Val	Thr	Gln	
785					790					795					800	
Leu	Met	Pro	Tyr	Gly	Cys	Leu	Leu	Asp	His	Val	Arg	Glu	His	Arg	Gly	
				805					810					815		
Arg	Leu	Gly	Ser	Gln	Asp	Leu	Leu	Asn	Trp	Cys	Val	Gln	Ile	Ala	Lys	
			820					825						830		
Gly	Met	Ser	Tyr	Leu	Glu	Glu	Val	Arg	Leu	Val	His	Arg	Asp	Leu	Ala	
		835					840					845				
Ala	Arg	Asn	Val	Leu	Val	Lys	Ser	Pro	Asn	His	Val	Lys	Ile	Thr	Asp	
	850					855					860					
Phe	Gly	Leu	Ala	Arg	Leu	Leu	Asp	Ile	Asp	Glu	Thr	Glu	Tyr	His	Ala	
865					870					875					880	
Asp	Gly	Gly	Lys	Val	Pro	Ile	Lys	Trp	Met	Ala	Leu	Glu	Ser	Ile	Leu	
			885						890					895		
Arg	Arg	Arg	Phe	Thr	His	Gln	Ser	Asp	Val	Trp	Ser	Tyr	Gly	Val	Thr	
			900					905					910			
Val	Trp	Glu	Leu	Met	Thr	Phe	Gly	Ala	Lys	Pro	Tyr	Asp	Gly	Ile	Pro	
		915					920						925			
Ala	Arg	Glu	Ile	Pro	Asp	Leu	Leu	Glu	Lys	Gly	Glu	Arg	Leu	Pro	Gln	
	930					935					940					
Pro	Pro	Ile	Cys	Thr	Ile	Asp	Val	Tyr	Met	Ile	Met	Val	Lys	Cys	Trp	
945					950					955					960	
Met	Ile	Asp	Ser	Glu	Cys	Arg	Pro	Arg	Phe	Arg	Glu	Leu	Val	Ser	Glu	
			965						970					975		
Phe	Ser	Arg	Met	Ala	Arg	Asp	Pro	Gln	Arg	Phe	Val	Val	Ile	Gln	Asn	
			980					985					990			
Glu	Asp	Leu	Gly	Pro	Ser	Ser	Pro	Met	Asp	Ser	Thr	Phe	Tyr	Arg	Ser	
		995					1000					1005				
Leu	Leu	Glu	Asp	Asp	Asp	Met	Gly	Glu	Leu	Val	Asp	Ala	Glu	Glu	Tyr	
	1010					1015					1020					

Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Ala Leu Gly Thr
1025 1030 1035 1040

Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Ala Arg Ser Gly
1045 1050 1055

Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Pro Pro
1060 1065 1070

Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
1075 1080 1085

Gly Asp Leu Ala Val Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
1090 1095 1100

His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
1105 1110 1115 1120

Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
1125 1130 1135

Gln Pro Glu Tyr Val Asn Gln Pro Glu Val Arg Pro Gln Ser Pro Leu
1140 1145 1150

Thr Pro Glu Gly Pro Pro Pro Pro Ile Arg Pro Ala Gly Ala Thr Leu
1155 1160 1165

Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
1170 1175 1180

Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Ala Pro
1185 1190 1195 1200

Arg Ala Gly Thr Ala Ser Gln Pro His Pro Ser Pro Ala Phe Ser Pro
1205 1210 1215

Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
1220 1225 1230

Pro Pro Pro Ser Thr Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
1235 1240 1245

Tyr Leu Gly Leu Asp Val Pro Val
1250 1255

<210> 15

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:PCR primer
PDM-251

<400> 15

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32

<210> 16
<211> 33
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:PCR primer
PDM-279

<400> 16
ctggactcga gtcattagcg gtgcctgtgg tgg

33

<210> 17
<211> 32
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW028 hECD-PD
sense primer with NcoI site

<400> 17
gggcatggg gagcacccaa gtgtgcaccg gc

32

<210> 18
<211> 31
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW029 hECD-PD
antisense primer with XhoI site without stop

<400> 18
gggctcgagc actggcacgt ccagaccag g

31

<210> 19
<211> 35
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW038 primer
for site-directed mutagenesis

<400> 19
ggcccctcca gcccgatgga cagcaccttc taccg

35

<210> 20
<211> 35
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW039 primer
for site-directed mutagenesis

35

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<220>
<223> Description of Artificial Sequence:AW036 sense
primer with NcoI site
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28

<220>
<223> Description of Artificial Sequence:AW037 antisense
primer with XhoI site

60

<220>
<223> Description of Artificial Sequence:Ra12.JC05 PCR
fragment

33

<220>
<223> Description of Artificial Sequence:Ra12.JC06 PCR
fragment

29

32

<220>

<223> Description of Artificial Sequence:LeIF.JC03 PCR
fragment

<400> 25

cgcccatggc gcagaatgat aagatcgccc

30

<210> 26

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LeIF.JC04 PCR
fragment

<400> 26

gccccatggc gtcgcatg aactttctcg tc

32

00854356-050901